Amoxicillin vs Levofloxacin in Treatment of Chronic Periodontitis: Review

Samara M. Ali.
Basic Science Dept. College of Dentistry, Baghdad univ.
Sarmad M. H. Zeiny
Dept. of Microbiology. College of medicine Baghdad univ.

ABSTRACT

Background: Antibiotics Resistance can be the main problem faced by the specialists in the medical fields. The main reason of such resistance is the improper prescribing of antibiotics. In dentistry this problem must be in concern for 2 reasons, first, limited and outdated knowledge of many dentist in Iraq with recent modalities in the field of therapeutics, so they keep prescribing penicillins, for every odontogenic infection (rationale prescribing), second, the patient who keeps prescribing the same drug for himself every time (i.e. dealing with antibiotic as over-the-counter drug).

Aim of the study: This review will clarifies the use of amoxicillin (most prescribed drug in Iraqi dental clinics) vs the use of third generation quinolones (levofloxacin) in an important field of dental practice which is periodontology, with focusing on levofloxacin as it took a privileged position in medical researches.

Conclusion: levofloxacin was superior to amoxicillin since it is applied once daily, few nonhazardous side effects, nearly 100 % bio-availability in spite of different rout of administration, and can be applied topically as gels and intra- pocket films. Perhaps this can change a lot among practitioners' and non- practitioners' prescribing (habits).

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INTRODUCTION

Infection is a major category of human illness and skillful managing of antimicrobial drugs is of the first rank [1]. The challenge is made more difficult by the problem of emerging resistances and socio-economic status that is on decline [2].

Dental infections are polymicrobial involving a combination of gram positive, gram negative, facultative anaerobes, and strict anaerobic bacteria [3]. While there are many antibiotic preparations offered for the treatment of localized and systemic infections, comparatively few antibiotic preparations are routinely engaged in dentistry [4].

Dentists prescribe medications for the management of a number of oral conditions, mainly orofacial infections [5]. The prescribing of antibiotics by dental practitioners has become an important aspect of dental practice. For this reason, antibiotics account for the bulk of medicines prescribed by dentists [6].

The accidental discovery of a mould called "Penicillium Notatum" which had the potential of inhibiting Staphylococcus colonies by Alexander Flemming in 1928 paved the way for the miracle drug "Penicillin" which saved millions of lives and opened a new era of curative medicine [7].

Penicillins can be classified into four broad categories, each covering a different spectrum of activity. The natural penicillins (penicillin G and penicillin V) have activity against many gram-positive organisms, gram-negative cocci, and some other gram-negative organisms. The aminopenicillins (ampicillin, amoxicilline, bacampicillin, and pivampicillin) have activity against penicillin-sensitive gram positive bacteria, as well as Escherchia coli, Proteus mirabilis, Salmonella sp., Shigella sp. and Haemophilus influenza. The antistaphylococcal penicillins (cloxacillin, dicloxacillin, etc) are also active against beta - lactamase - producing staphylococci. The antipseudomonal penicillins have less activity against gram positive organisms than the natural penicillins or aminopenicillins [8]. The penicillins are nontoxic and remarkably safe drug. The hypersensitivity reaction leading to anaphylaxis is the only major problem which is seen in approximately 5 to 10% of the patients taking penicillin. The minor adverse effects include nausea, vomiting, pain and inflammation at the site of injection after intramuscular administration has been reported [9].

Fluoroquinolones a class of man-made antibiotics. Over 10,000 fluoroquinolone analogs have been synthesized, including several with wide clinical presentations.

Fluoroquinolones in use nowadays typically offer greater efficacy, a broader spectrum of antimicrobial activity, and a better safety profile than their forerunners[1].

Levofloxacin (trade names: Levaquin, Advaquin, Tavanic, Levomed, Novotic which is widely spread in Iraqi market); Is a broad-spectrum antibiotic of

the fluoroquinolone drug class (third generation of quinolones) [10]. Its spectrum of activity includes most strains of bacterial pathogens responsible for respiratory, urinary tract, gastrointestinal, and abdominal infections, including Gram negative (Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Legionella pneumophila, Moraxella catarrhalis, Proteus mirabilis, and Pseudomonas aeruginosa), Gram positive (methicillin-sensitive but not methicillinresistant Staphylococcus aureus, Streptococcus pneumoniae, Staphylococcus epidermidis, Enterococcus faecalis, and Streptococcus pyogenes), and atypical bacterial pathogens (Chlamydophila pneumoniae and Mycoplasma pneumoniae).

Compared to earlier classes such as ciprofloxacin, levofloxacin exhibits greater activity towards Gram-positive bacteria [11].

Most adverse reactions are mild to moderate; yet, sometimes serious adverse effects occur. There is some disagreement in the medical literature regarding whether and to what extent levofloxacin and other fluoroquinolones produce serious adverse effects more frequently than other broad spectrum antibacterial drugs [12, 13,14].

This review shed the light over the use of both penicillins and levofloxacin in an important field of dental practice which is periodontology.

Amoxicillin

In 2003 martin Addy reported that chronic inflammatory periodontal conditions are not indicated for antibiotics; systemic antimicrobials should only be used in acute periodontal conditions where drainage or debridement is impossible, where there is local spread of the infection or where systemic upset has occurred. The disadvantages of systemic antimicrobials can be grouped under the headings of allergic reactions, superinfection, toxicity, drug interactions, and patient compliance and, perhaps of most widespread importance, bacterial resistance [15].

In 2006 N. J. Lopez et al reported that the effect of metronidazole plus amoxicillin as the sole therapy, on the sub gingival microbiota of chronic periodontitis. This was confirmed in a study held with twenty-two patients with untreated chronic periodontitis were randomly assigned to a group that received a combination of amoxicillin plus metronidazole for 7 days, and a group receiving scaling and root planning and two placebos [16].

In 2013 Anna K. Szkaradkiewicz and Tomasz M. Karpiński described Periodontitis as a chronic oral infection that lead to rapid destruction of periodontal tissues. On the development of the disease have an impact many bacteria, in particular anaerobic bacteria which act on fibroblasts, epithelial and endothelial cells and extracellular matrix components [17]. This leads to the conclusion that amoxicillin have no effect in managing chronic periodontitis comparing with metronidazole which affects anaerobic cocci, and anaerobic gram-negative bacilli [1].

Levofloxacin

In 1998 H. M. Wexler et al reported an important paper that compared the effect of levofloxacin with ofloxacin, ciprofloxacin, ampicillin, sulbactam , cefoxitin, and metronidazole for a selected group of anaerobes isolated from skin and soft tissue infections, and the final conclusion was that Levofloxacin has good activity against certain groups of anaerobic isolates (non-B. fragilis Bacteroides species, Veillonella species, Prevotella species, and Porphyromonas species)[18].

In 2003 Stein G. E. , Goldstein EJ. In a review confirmed that in clinical efficacy trials, levofloxacin has been effective in the treatment of patients with gynecologic, skin and skin-structure, and bone infections involving anaerobic pathogens [19].

In 2014 Avani R. Pradeep et al held a study on sixty five patients with chronic periodontitis randomly divided into test and control group in which the test group was treated with oral levofloxacin 500 mg once daily. Results showed that Patients receiving levofloxacin showed statistically-significant improvements in mean probing depth and clinical attachment level. The conclusion was confirmed at last that levofloxacin has significantly improved the clinical and microbiological parameters of chronic periodontitis [20].

In 2013 B. M. Borole et al formulated a levofloxacin hemihydrate in - situ oral gel to be applied without incision. This was developed by using various concentrations of plaxomer which exhibit sol- to- gel phase transition converting to gel at body temperature 37C° from liquid at room temperature 25 C°, each formulation was evaluated with various parameters such as physiochemical properties, viscosity, gelation properties, gelation temperature, spreadability, in vitro release and stability. The results were satisfactory for all formulations but they recommended to use polymers instead for more bioavailability [21].

Later in 2014 Neha Bisht et al directed their efforts to formulate and evaluate in situ oral topical gels of levofloxacin. In-situ gel were prepared by using carbopol 934P and using sodium carboxy-methyl cellulose along with hydroxyl-propylmethyl-

cellulose was used to prolong the release of levofloxacin. Formulations were evaluated for gelling capacity, viscosity, gel strength, bio-adhesive force, spreadability, microbiological studies and in vitro release. Levofloxacin from the muco-adhesive system in simulated salivary fluid was influenced significantly by the properties and concentration of carbapol 934 and sodium CMC showed to enhance bioavailability through its longer oral residence time and ability to sustain the release of the drug. The gels which was prepared by using the technique thermo reverse gelation with Levofloxacin shown good antimicrobial activity. The In situ systems showed increased residence time and prolonged drug release for over 8 hrs.

Conventional oral formulations like solution, suspension, and ointments have many disadvantages which result into poor bioavailability of drug.[22].

As intra pocket medication; In 2010 Prabushankar GL, Gopalkrishna B, Manjunatha KM, Girisha CH has formulated and evaluated Levofloxacin dental films for Periodontitis. Films were prepared by solvent casting technique.

Periodontal films containing Levofloxacin were prepared. In vitro characterization studies revealed that Levofloxacin can be integrated in a slow release device for the treatment of periodontitis. Ageing studies shows that the drug remained intact and stable in the periodontal films during storage. Spectroscopic data shows there is no significant chemical interaction between the drug and polymers. Further, detailed investigation is required to establish in vivo efficiency of these films[23].

CONCLUSION

It is observable that levofloxacin is not only preferred over penicillins it is also preferred even over newer (4th) generation quinolones this is due to its broad spectrum of activity.

Antibiotic spectrum:

Levofloxacin has excellent activity against G- negative bacilli. Amoxicillin is a wide-spectrum antibiotic but it is not effective against gram negative bacilli so metronidazole is added in many therapeutic regimens [16].

Bioavailability and dosage forms:

Levofloxacin is available in the market as a conventional dosage forms such as tablets, capsules, and parenteral for the treatment of bacterial infections [23]. It is rapidly and completely absorbed after oral administration, with a plasma concentration profile equal to that obtained from intravenous administration of the same amount (bioavailability 100% compared with 60- 70% for oral penicillins), oral fluoroquinolones should be taken 2 hours before or 4 hours after antacids[24] .

This is definitely preferred by patient instead if confusing multi- application of amoxicillin (3time) during the day. Most of the penicillins are incompletely absorbed after oral administration, and they reach the intestine in sufficient amounts to affect the composition of the intestinal flora. Food decreases the absorption of all the penicillins because as gastric emptying time increases, the drugs are destroyed by stomach acid. Therefore, they should be taken on an empty stomach [25].

Topical forms of levofloxacin (gels and intra-pocket films) revealed chemical stability during preparation, storage and application; yet no topical penicillins are seen.

Side-effects:

In general, levofloxacin is well tolerated; but like most antibiotics, the most common adverse effects of fluoroquinolones are nausea, vomiting, and diarrhea.

Headache and dizziness or light- headedness may occur, should be avoided in pregnancy and in nursing mothers, and in children under 18 years of age, because of articular cartilage erosion (arthropathy and tendinitis), should not be used in patients who are predisposed to arrhythmias or are taking antiarrhythmic medications. Still penicillins are among the safest drugs.. However neurotoxic, nephrotoxic, cation toxicity (hypokalemia) is likely to occur among susceptible patients [1, 13, 14, 25].

Combination:

The antibiotics prescribed most commonly by dentists either amoxicillin alone or in addition to metronidazole. [26, 27] while levofloxacin prescribed alone.

Allergy:

Among the most important problems in penicillins is allergy. Allergic reactions include anaphylactic shock (0.05% of recipients); serum sickness-type reactions (urticaria, fever, joint swelling, angioneurotic edema, intense pruritus, and respiratory compromise occurring 7 –12 days after exposure); and a variety of skin rashes [24]. Levofloxacin could be the safer among first-, second- or fourth-generation quinolones in cases of allergic reaction [28].

Resistance:

Resistance to any drug obtained due to:

1. Repetitive prescription by practitioners and / or non- practitioners (volume of drug use).
2. Exposure of bacteria to low concentration of

antibiotic.

3.Absence of knowledge of cross- resistance [29].

Resistance to penicillins and other β-lactams is due to one of the following mechanisms: (1) inactivation of antibiotic by β-lactamase, (2) modification of target penicillin- binding proteins, (3) impaired penetration of drug to target penicillin binding proteins.

Beta-lactamase production is the most common mechanism of resistance (24). In quinolones, resistant organisms emerge only due to one or more point mutations in the quinolone binding region of the target enzyme or to a change in the permeability of the organism, (28), this limited the resistance only in streptococcus pneumonia, which is not related to oral conditions [30] .

RECOMMENDATIONS

After reviewing this article we recommend that:-

1.Dentists must be routinely updated with advances in field of therapeutics.

2.Proper diagnoses and analysis will definitely lead to proper drug prescribing.

3.Antibiotics should not be consumed as OTC (over the counter drugs). This can be limited in Iraq by using the system of bar code so the patient will be prevented from re- dispensing the prescription once again (rationale use).

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